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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
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BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

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**Office Action Summary**

Application No.

09/782,004

Applicant(s)

DAHIYAT ET AL.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

**A. SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 03/09/05.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 12,13,21-24 and 33-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12,13,21-24 and 33-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Status of Claims***

1. Amendment filed 03/09/05 is acknowledged. Claims 31-35 are added. Claims 12,13,21-24,33-35 are pending.
2. During the subsequent interview conducted on 05/24/2005, after an extensive discussion of utility issues, it was agreed that applicant would further consider amendments to the claims and specification to resolve the issues of the utility of invention, and therefore, the next Office action would defer addressing these issues until the next applicant's response.

### ***Specification: Incorporation by reference***

3. Applicant submits that various ways of calculating forcefield are not essential material to describe the claimed method because any of them can be used equally successfully.

### ***Claim Rejections - 35 U.S.C. § 101/ 112-1***

4. Claims 12,13,21-24,33-35 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

As stated above, the discussion of this rejection is deferred until the next applicant's response.

***Claim Rejections - 35 USC § 112, second paragraph.***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 12,35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims introduce proviso that "at least one of secondary variant proteins is different from primary variant proteins". There is no antecedent basis for the term "primary variant proteins" because all the preceding part of the claim addresses is primary variant amino acid residues, not proteins.

***Claim Rejections - 35 USC § 102 and 103 .***

6. Claims 12,13,33-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Lacroix et al (US 2002/0072864; filing date 08/31/1999).

The rejection is re-stated in view of claims amendments removing the step of generating probability distribution table and in view of submission of new claims

The claims are drawn to method for generating a secondary library of target protein comprising:

- a) inputting three-dimensional coordinates of the target protein into a computer;
- b) utilizing forcefield calculation to generate primary library comprising a plurality of primary variant amino acid residues at primary variant positions, and ;
- c) combining a plurality of said primary variant amino acid residues from step b) to generate a secondary library of secondary variant proteins.

In addition, independent claims 12, 35 further limit step with proviso that "at least one of secondary variant proteins is different from primary variant proteins.

US 2002/0072864 teaches computer-based method for macromolecular engineering wherein the method comprises steps of

- a) inputting coordinates of said protein into a computer (see, e.g., claims 12,13);
- b) using various force field calculations (see sections 5.4.1; 5.8.1; 5.9.2)
- c) combining, after subsequent steps, candidates for the target structures (see section 5.11).

With respect to limitation of claims 12,35, that at least one of secondary variant proteins is different from primary variant proteins, Lacroix's method considers "the immense variety of sequences that can be generated as a result of protein mutagenesis, i.e., substitution of one amino acid side chain with a different amino acid side chain at a given site in the protein". Thus, the resulting set can be different from original variant.

It is the Examiners position that all the elements of Applicant's invention with respect to the specified claims are instantly disclosed by the teaching of the reference cited above. Note that claim 12 is amended to remove the step of computationally generating probability distribution table; the same lack of this step is the new claim 34.

Response to arguments

Applicant argues that Lacroix reference does not offer direct connection between the method steps discussed in the rejection. Neither, however, such connection is offered by the claimed method, which, in the amended version addresses, offers only one computational step – use of forcefield calculation. In addition, the claim language is open-ended “comprising” which allows for any other unspecified method steps.

Applicant further argues that the reference does not address “primary” and “secondary” library in the sense meant by the specification. The claims, however, are addressed to their maximum breadth, and both “primary” and “secondary” library are viewed simply as collections of amino acid residues. The features of neither of these libraries are recited in the claims (as was suggested during the interview with applicants). In addition, the results of the computational steps of Lacroix is a subset of optimized structures, which conforms to the definition of the applicant.

7. Claims 21-24 remain rejected under 35 U.S.C. 103(a) as obvious over Lacroix et al (US 2002/0072864; filing date 08/31/1999). The reference teaches synthesizing candidate structure(s) (see, e.g., claim 158). Although the reference does not teach specifically PCR method, such conventional method of protein synthesis would be an obvious choice to an artisan.

Response to arguments

Applicant argues that Lacroix is merely synthesizing a small number of variant sequences that would be “worthy of synthesis”. It is Examiner’s understanding that the objective of claimed method, as well as of the method of Lacroix, as well of other computational design methods, is to carry out majority of design and selection steps *in silico* and to synthesize only sequences that would be “worthy of synthesis”. As to the

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use of the PCR, Examiner maintains that as it is a conventional method of protein synthesis, use of PCR would be an obvious choice to an artisan.

### ***Double Patenting***

8. Double-patenting rejection of claims 12,21-24 over claims 1-8 of U.S. Patent No. 6,403,312 is withdrawn in view of Terminal Disclaimer filed 05/09/2005.

9. Claims 12, 21-24, 33-35 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-21 of copending Application No. 09/927790 in view of Wang et al (Pub. Med ID 8862547; Protein Engineering, 9(6),479-484, 1996) or Ulrich et al (Proteins: Structure, Function, and Genetics, 27,367-384, 1997).

Applicant requests that the rejection is reevaluated once the claims of both applications are in condition for allowance.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marshel, Ph.D., can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Michael Borin, Ph.D.  
Primary Examiner  
Art Unit 1631

7/22/05